UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/705,618 | 11/10/2003 | Lynn E. Spitler | 204372000902 | 4690 |

25225 7590 12/27/2005

MORRISON & FOERSTER LLP
12531 HIGH BLUFF DRIVE
SUITE 100
SAN DIEGO, CA 92130-2040

| EXAMINER | |
|---|---|
| HUMPHREY, DAVID HAROLD | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1643 | |

DATE MAILED: 12/27/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/705,618 | SPITLER ET AL. | |
| | Examiner | Art Unit | |
| | David Humphrey | 1643 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *10 November 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *54-62* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *54-62* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3/15/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

1. The Office acknowledges the receipt of Applicant's Amendment to the claims, filed on 11/10/2003. Claims 54-62 are added. Claims 1-53 are canceled.

2. Claims 54-62 are pending.

3. Claims 54-62 are examined on the merits.

### *Specification*

4. Applicant is required to update the status (pending, allowed, etc.) of all parent priority applications in the first line of the specification. The status of all citations of US filed applications in the specification should also be updated where appropriate.

### *Information Disclosure Statement*

5. An initialed and dated copy of Applicant's IDS form 1449, filed 3/15/2004, is attached to the instant Office action.

### *Claim Rejections - 35 USC § 112, first paragraph*

6. The following is a quotation of the first paragraph of 35 U.S.C. §112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 54-62, are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating a subject by administration of an anticancer agent, CPT-11, and JBT3002 in multilamellar vesicles to reduce intestinal

damage (intestinal mucositis) does not reasonably provide enablement for a method of treating a subject with any **neoplastic** agent and JBT3002 to alleviate or prevent any side effects including myelosuppression, oral mucositis, esophageal mucositis, and peripheral neuropathy. The specification is also not enabling for a method of treating a subject by administration of any **anti-neoplastic** agent and JBT3002 to reduce intestinal damage (intestinal mucositis). Further, the specification is not enabling for "prevention" of side effects. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir,1988). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue' not 'experimentation'. " (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the breadth of the claims, (2) the nature of the invention, (3) the state of the prior art, (4) the level of one of ordinary skill, (5) the level of predictability in the art, (6) the amount of direction provided by the inventor, (7) the existence of working examples, (8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

*The breadth of the claims and the nature of the invention:* The claims are directed to a method of alleviating or preventing side effects in a subject selected from the group consisting of myelosuppression, mucositis, and peripheral neuropathy that are associated with treatment with either a neoplastic or anti-neoplastic agent. The claimed method requires the administration of JBT3002 (N-palmitoyl-S-[2(R,S), 3-dilauroyloxy-propyl]-(R)-cysteine) in an amount sufficient to alleviate or prevent said side effect. The claims also recite encapsulating JBT 3002 in liposomes and more specifically multilamellar liposomes.

*The state of the prior art and predictability in the art:* Those of skill in the art recognize that neoplastic and anti-neoplastic agents have different modes of action and different side effects associated with their use. In addition, one of skill in the art would recognize that while it is possible to reduce or alleviate unwanted side effects, it is another matter to prevent side effects of chemotherapy.

There are many anti-neoplastic agents available including chemotherapy drugs as well as non-chemotherapy medications such as interferon and interleukin (called biological therapies) and monoclonal antibodies (such as Herceptin and Rituxan). Anti-neoplastic agents have potential and specific side effects associated with them, as well as the more general side effects of the treatment. At the time of filing, the prior art demonstrates that treating cancer by administering a combination of anti-neoplastic agents was not routine. Smorenburg et al. (European Journal of Cancer 37: 2310-2323 (2001)) teach that combining two chemotherapeutic agents is not simply a matter of putting antitimour activities together. Drug interactions may result in synergism, no only

of efficacy, but also of toxic side-effects. Adding two drugs may also cause antagonism in drug efficacy due to unwanted interference in cytotoxicity or pharmacokinetics, see page 2319, right column, lines 1-6.

In summary, the prior art teaches that treating any type of cancer with a combination of agents is not routine, one of ordinary skill in the art would require a significant amount of guidance in the specification as well as the presence of working examples to practice the invention as claimed.

*Amount of direction provided by the Inventor and existence of working of working examples:* The applicant has not demonstrated sufficient guidance provided in the form of adequate supporting representation or art recognized correlations in patent or non-patent literature to support the full scope of the claims. Applicant discloses the use of one anti-neoplastic agent, CPT-11, in combination with JBT3002 to reduce CPT-11-induced intestinal damage of C57/BL/6 mice (see Specification page 52, Example 8 and corresponding Figure 21; page 60, Example 14, and corresponding Figure 22). However, the data presented in Figures do not conclusively show that intestinal side effects have been prevented. In addition, there was no demonstration of reduction of either oral or esophageal mucositis. The specification also does not include working examples that combine JBT3002 with any anti-neoplastic agent or neoplastic agent to alleviate myelosuppression and peripheral neuropathology.

A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the

claimed inventions without undue experimentation. In re Wright, 27 USPQ2d 1510 (CAFC). The disclosure does not demonstrate sufficient evidence to support the applicants' claim to alleviating myelosuppression, peripheral neuropathy, and mucositis in any subject by administration of JBT3002 and any anti-neoplastic agent. All of the factors considered in the sections above, underscores the criticality of providing working examples in the specification for an unpredictable art such as providing gene therapy to animals to treating cardiovascular diseases.

*Quantity of experimentation needed to make or use the invention based on the content of the disclosure:* In view of the Wands factors considered above, one of ordinary skill in the art would conclude that utilizing the method of treating a subject with a neoplastic agent and JBT3002 to alleviate any side effects including myelosuppression, mucositis, and peripheral neuropathy, would require undue experimentation in order to practice the invention as claimed by the Applicants.

## ***Conclusion***

8. No claim is allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Humphrey whose telephone number is (571) 272-5544. The examiner can normally be reached on Mon-Fri 8:30AM-5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

David Humphrey, Ph.D.

December 6, 2005

LARRY R. HELMS, PH.D.
SUPERVISORY PATENT EXAMINER